

WHAT IS CLAIMED IS:

1. A method of promoting fatty acid oxidation and weight loss in an individual, comprising the step inhibiting the activity of acetyl-CoA carboxylase 2 in said individual.

2. The method of claim 1, wherein said activity is inhibited by administration of an inhibitor of acetyl-CoA carboxylase 2 (ACC2) to said individual.

3. The method of claim 1, wherein said individual has a pathophysiological condition.

4. The method of claim 3, wherein said pathophysiological condition is selected from the group consisting of obesity and diabetes.

5. A method of decreasing blood sugar in an individual, comprising the step of administering an inhibitor of acetyl-CoA carboxylase 2 (ACC2) to said individual.

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6. The method of claim 5, wherein said individual has diabetes.

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7. A transgenic mouse, said mouse comprising a mutation in an endogenous ACC2 gene for the acetyl-CoA carboxylase 2 isoform of acetyl-CoA carboxylase, wherein said mutation inactivates said gene and results in the lack of expression of a functional acetyl-CoA carboxylase 2 isoform.

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8. The mouse of claim 7 wherein one or more exons of said ACC2 gene has been deleted.

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9. The mouse of claim 8, wherein said exons have been replaced with heterologous DNA sequences.

5 10. The mouse of claim 9, wherein said heterologous DNA sequences comprise an hypoxanthine phosphorylribosyltransferase expression cassette.

10 11. The mouse of claim 10, wherein an exon encoding a biotin binding motif of ACC2 is replaced with an hypoxanthine phosphorylribosyltransferase expression cassette.

15 12. The mouse of claim 7, wherein said mouse exhibits a phenotype comprising a metabolic reduction in malonyl-CoA production in skeletal muscle and heart.

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13. The mouse of claim 12, further comprising a phenotype of unrestricted fat oxidation and reduced fat accumulation in the liver and fat storage cells.

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14. The mouse of claim 13, further comprising a phenotype of consuming more calories than a wild-type mouse, yet accumulating less fat than a wild-type mouse.

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15. A method of screening for an inhibitor of acetyl-CoA carboxylase 2 isoform activity comprising the steps of:

administering potential inhibitors to wild-type mice; and,

screening for mice which exhibit the phenotype of the

15 transgenic mouse of claim 14.

16. An acetyl-CoA carboxylase 2 inhibitor identified by the method of claim 15.

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17. A pharmaceutical composition comprising the acetyl-CoA carboxylase 2 inhibitor of claim 16 and a pharmaceutically acceptable carrier.

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18. A method of obtaining a purified preparation of acetyl-CoA carboxylase 1 protein which is free of acetyl-CoA carboxylase 2 comprising the step of:

purifying said acetyl-CoA carboxylase 1 protein from
10 tissues obtained from the transgenic mouse of claim 7.

19. A method of obtaining murine antibodies against acetyl-CoA carboxylase 2 which are less crossreactive with acetyl-
15 CoA carboxylase 1 and other mouse proteins comprising the step of:

generating said antibodies in the transgenic mouse of claim 7.

20 20. A cell line derived from the transgenic mouse of claim 7.

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21. The cell line of claim 20, wherein said cell line is derived from cells selected from the group consisting of muscle cells, heart cells, adipose cells, and liver cells.

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22. A method of screening for agonists and antagonists of ACC2 comprising the steps of:

administering a candidate compound to the cell line of
10 claim 20 and to cell lines derived from wild-type mice; and,

monitoring said cell lines for alterations in cellular activity, wherein a compound that specifically acts on ACC2 will have altering cellular activity in wild-type cells but will have no effect on the cell line of claim 20.

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23. The method of claim 22, wherein monitored cellular activities are selected from the group consisting of mRNA expression, protein expression, protein secretion, and lipid metabolism.